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REACTIONS OF ABIETIC ACID METHYL ESTER WITH m-CHLOROPERBENZOIC ACID

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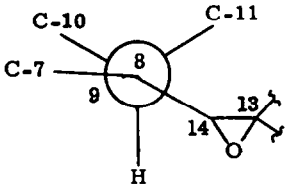
Abstract - Abietic acid methyl ester reacts regioselectively with m-chloroperbenzoic acid, in the presence of water to yield a mixture of the two epimeric 13,14-monoepoxides. These epoxides further react affording a mixture of 1,2- and 1,4-unsaturated diols. The overall yield of the reaction is acceptably good (70-80%). The formation of these and other products are discussed.

In the last few years we have been interested in the study of possible regioselective reactions[1] of abietic acid methyl ester (1). Surprisingly, though the epoxidation of conjugated dienes has been occasionally studied[2-4], that of abietic acid or methyl abietate is not well documented. A first report[5] indicated the formation of a monoepoxide, as a very minor product of the photooxidation of 1. These authors[5] assign the α-configuration to this compound. Later reports point to the formation of several epoxides[6] (no further characterization) or disclose the preparation of epoxides and diols, in unstated yields, by treatment of methyl abietate with peracetic acid. The stereochemistry assigned to these products[7], apparently based on a correlation with the first reported epoxide[5] has not, in our opinion, been established on a firm base.

We report here the results obtained by the reaction of m-chloroperbenzoic acid (m-CPBA) with methyl abietate in neutral and acid media.

Initial experiments, using a stoichiometric amount of m-CPBA in anhydrous dichloromethane at 0° C led to the isolation of 13β, 14β- and 13α, 14α-monoepoxides (2 and 3) in modest yield only (20%, 2:1 ratio). Epoxide 2 was a solid[23], m.p. 60-62° C; (^{1}H NMR: 3.10, s, 14-H; 5.80, m W½ 9 Hz, 7-H). Epoxide 3 was also a solid, m.p. 66-70° C; (^{1}H NMR: 3.10, s, 14-H; 5.90, m W½ 6 Hz, 7-H). The configuration of the oxirane ring was established considering the chemical shifts assigned to C-9 and C-11 in the ^{13}C NMR spectra of both substances. These assignments reverse those previously made[5,7].

It is well established[8] that the epoxy group on a six-membered ring has an effect on the homoallylic carbon (γ from oxygen) bearing an axial hydrogen atom. If the epoxide oxygen and the axial hydrogen in the γ position are cis to one another the carbon atom bearing the hydrogen is always strongly shielded (3.5 - 6.0 ppm). However, in the case of trans relationship, the chemical shift of the γ carbon is only slightly affected. This steric effect is reflected in the chemical shift changes of C-9 from 1 to 3 and C-11 from 1 to 2, such as it could be expected from the corresponding diagrams[8b]:



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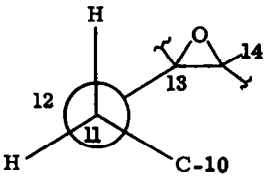
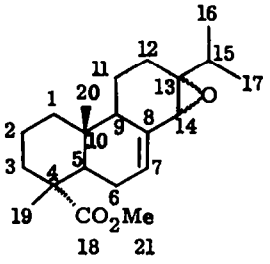


2

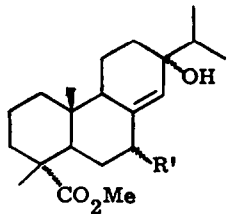
The total yield of these two epoxides could be slightly improved adding anhydrous sodium carbonate or potassium fluoride[9] to the reaction media (see Experimental). It appears that the 13,14-double linkage of 1 is richer in electrons than the 7,8-double bond. This is in agreement with the result obtained in the OsO_4 dihydroxylation of methyl abietate. The reaction occurs preferentially on the former bond yielding the 13 β-14 β-dihydroxyderivative[24]. Epoxide formation has electronic and steric requirements similar to those of the osmylation reaction. Consequently, the formation of the 13 β,14 β-epoxide (2) as the major reaction product should be reasonably expected.

Other substances[10] were present in the crude reaction product, most prominent among them were mixtures of dehydroabietic acid methyl ester and unidentified dienes (UV and NMR evidence), and m-chlorobenzoyloxy-derivatives corresponding to the acid opening of these epoxides. No diepoxides or only trace amounts could be detected. The starting material have completely dissapeared during the reaction.

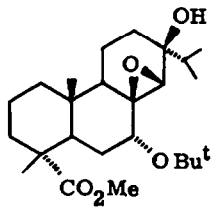
It was already apparent that the initial epoxides underwent a series of fast reactions leading to complex mixtures of compounds. In order to elucidate some of these possible pathways and help to the identification of the reaction products, the solvolysis of the epoxides 2 and 3 was then undertaken.



2 β-epoxide
3 α-epoxide



7 R' = α-OH 13 β-OH
8 R' = α-OBu^t 13 β-OH
10 R' = α-OBu^t 13 α-OH



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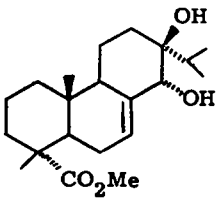

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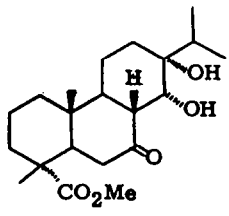

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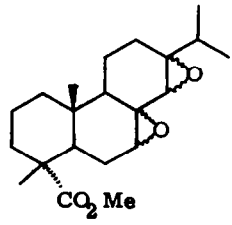


17 7,8 α-epoxide; 13,14 β-epoxide
18 7,8 β-epoxide; 13,14 α-epoxide
19 7,8 α-epoxide; 13,14 α-epoxide

The reaction of 2 with 0.12 N perchloric acid in t-butanol (2 : 98 v/v) at 0°C afforded a mixture of three substances (increasing R_F value order): methyl 7α, 13β-dihydroxy-abietate (7), methyl 13β, 14α-dihydroxy-abietate (4), and methyl 7α-t-butoxy, 13β-hydroxy-abietate (8).

The ^{1}H NMR spectrum of the diol 4, a new compound, showed the vinylic proton signal as a broad multiplet centered at δ 5.75 and the C-14 proton signal occurred as a sharp singlet at δ 3.85. Three signals at 74.01, 76.45 and 47.64 ppm of the ^{13}C NMR spectrum of 4 were assigned to C-13, C-14 and C-9 respectively. Comparison of this latter value with those published[11] for the two isomeric 14-hydroxy-derivatives of methyl isopiramate suggested an α-configuration of the C-14 hydroxyl group of 4. A similar analysis showed that the C-7 hydroxyl or t-butoxyl groups of compounds 7 and 8 had an α-configuration. The ^{13}C NMR spectra of both compounds showed the predictable γ-gauche effect on the chemical shifts of C-9 (47.26 and 47.07 ppm respectively) and C-5 (41.83 and 42.07 ppm respectively) (see Table 1) as it has been observed in the case of 7α-hydroxy methyl pimarate when compared with methyl pimarate[11]. The ^{1}H NMR spectrum of compound 7 has signals at δ 4.20 (m, W½ 9 Hz) and 5.70 (br s, W½ 3 Hz) assigned to 7-H and 14-H respectively). Analogous signals at δ 3.90 and 5.55 appeared at the ^{1}H NMR spectrum of 8. An allylic stabilization[12] of the original carbocation seems to be responsible of the formation of compounds 7 and 8. The β-configuration of the C-13 hydroxyl group of 4, 7 and 8 was based on mechanistic grounds.[21] For the case of 4 it was also confirmed by using a chemical correlation with the previously described 13 β-hydroxy-14-oxo-abiet-7-en-18-oic acid[24].

Two products 5 and 10 were also isolated from the reaction of the 13α,14α-monoepoxide 3 with 0.12 N perchloric acid in identical conditions to those described above. The α-stereochemistry assigned to the C-14 hydroxyl group of the vicinal diol 5 was suggested by the observed chemical shift of C-9 in the ^{13}C NMR spectrum of this compound (46.77 ppm). The cis arrangement of the vicinal diol was confirmed by the formation of a complex with boric acid as evidenced by the ^{13}C NMR spectrum of 5 in pyridine-chloroform (1 : 1) solution saturated with boric acid[13]. 7-H and 14-H of compound 5 appeared as a multiplet (W½ 9 Hz) and a singlet at δ 5.70 and 4.00 respectively. Compound 5 has not been formed by a normal diaxial opening of the oxirane ring but through a stabilized allylic carbocation.[22]

Assignment of a 7α-configuration to the ter-butoxyl group of 10 followed from the observed γ-gauche effect on the signals assigned to C-5 and C-9. In fact the chemical shifts of the C-1 to C-7 carbon atoms of 10 were almost identical to those found for compound 8 (see Table 1). Analogous results were obtained when the solvolysis of epoxide 3 was carried out in tetrahydrofuran : water (10 : 1) with perchloric acid in catalytic amounts. Compounds 5 and 11 were isolated[21]. Compound 11 constituted almost 50% of the total yield. Its ^{1}H NMR spectrum exhibited two signals at δ 4.15 (m, W½ 6 Hz) and 5.65 (br s, W½ 3 Hz) assigned to 7-H and 14-H respectively. The ^{13}C NMR data (see Table 1) was also consistent with the stereochemistry assigned to this compound.

It was expected that the identification of all these products it would help us with the interpretation of the complex mixture which was obtained during the epoxidation of 1. Other possible reaction products could be diepoxides or epoxides of the diols obtained during the solvolysis reaction. Consequently, epoxide 2 was subjected to epoxidation with m-chloroperbenzoic acid in presence of anhydrous sodium carbonate. Although rather sluggishly, the reaction afforded diepoxide 17 (73% yield). The α-configuration of the new oxirane ring was suggested by the ^{13}C NMR data (see Table 2) and was consistent with the expected steric and electronic effects[14]. The reaction of epoxide 3 under identical conditions afforded a mixture of two diepoxides (18 and

Table 1. ^{13}C NMR chemical shifts (ppm) for hydroxycompounds and other derivatives.

	4	5	7	8*	10**	11	12	13***	16	20
C-1	39.1	38.8	38.2	38.1	38.1	37.8	37.8	37.9	37.8	38.7
C-2	18.1	18.0	18.1	18.2	18.3	18.2	17.9	17.8	17.8	17.7
C-3	37.3	37.0	37.0	36.3	36.3	36.9	36.8	36.6	36.4	36.7
C-4	46.6	46.5	46.9	47.3	47.4	47.0	47.2	47.4	47.0	46.2
C-5	45.2	44.8	41.8	42.1	42.4	42.2	48.0[b]	42.1	42.9	47.3
C-6	25.5	25.3	31.8	32.8	33.4	31.9	41.4	39.2[b]	30.1	39.7
C-7	125.2	127.3	72.6	71.7	71.8	72.3	211.4	72.0	71.3	205.4
C-8	140.8	138.0	144.0	144.4	142.0	140.5	48.4[b]	65.4	67.6	62.9
C-9	47.6	46.8	47.3	47.1	45.5	45.6	50.9[b]	46.3	40.7	43.9
C-10	34.9	34.7	37.8	37.7	38.8	38.4	36.0	37.5	38.7	37.2
C-11	19.6	20.1	17.0	17.0	17.9	18.1	21.2	13.6	15.4	17.4
C-12	29.1	28.7	30.0	29.7	31.2	31.9	29.9	30.5[b]	27.9	27.7
C-13	74.0	74.9	71.4	71.4	72.0	72.2	73.4	70.2	70.3	71.6
C-14	76.4	77.1	131.3	129.1	130.0	132.6	68.7	63.4	68.5	65.9
C-15	33.1	28.7	37.7	38.1	36.2	35.8	28.6	36.8	35.9	32.7
C-16	16.5	16.1[a]	16.6[a]	16.7[a]	17.0[a]	16.8[a]	16.2[a]	17.0[a]	17.1[a]	16.6[a]
C-17	16.5	15.9[a]	17.4[a]	17.3[a]	16.7[a]	16.7[a]	16.0[a]	16.5[a]	16.4[a]	16.5[a]
C-18	178.7	179.0	178.9	179.0	179.0	179.1	177.7	178.8	178.6	177.7
C-19	17.5	17.4	17.1	17.0	17.0	17.0	16.4[a]	17.1	17.2[a]	16.6[a]
C-20	15.4	15.1	14.4	14.4	15.0	15.0	13.8	14.9	17.8	16.2
C-21	52.0	51.9	52.0	51.7	51.7	52.2	52.2	51.8	52.1	52.2

[a, b] Reversed assignment is also possible.

* Signals for $O\underline{C}(CH_3)_3$ and $OC(\underline{C}H_3)_3$ occurred at 73.7 and 28.8 ppm respectively.

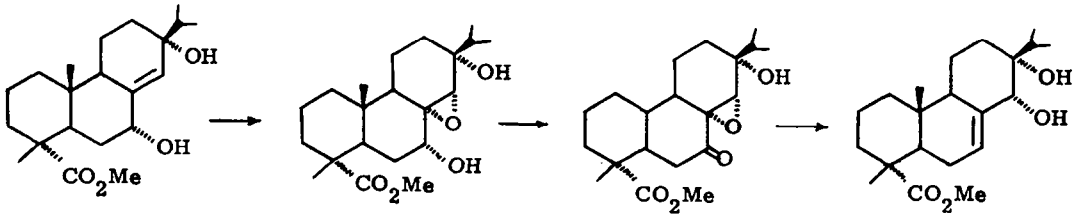
** Signals for $O\underline{C}(CH_3)_3$ and $OC(\underline{C}H_3)_3$ occurred at 73.7 and 28.9 ppm respectively.

*** Signals for $O\underline{C}(CH_3)_3$ and $OC(\underline{C}H_3)_3$ occurred at 73.6 and 28.8 ppm respectively.

19) (1:2 ratio, 76% overall yield). Apparently, here, steric reasons prevailed over electronic effects and the α,α-diepoxide was the main reaction product. ^{13}C NMR data of both substances gave an indication about the stereochemistry of the new oxirane ring.

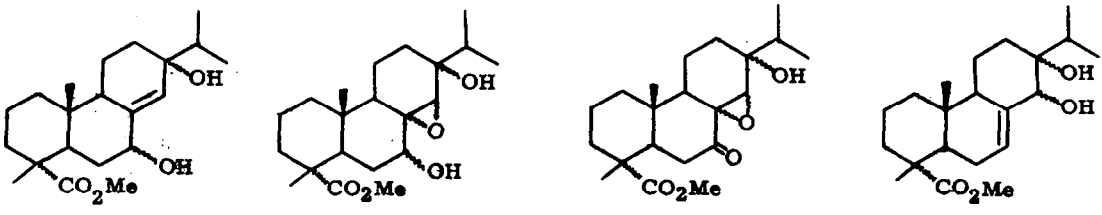
Two compounds 8 and 11 were also subjected to epoxidation with m-chloroperbenzoic acid. Compound 8 gave a single product 13 (88% yield). The β-stereochemistry assigned to the oxirane ring seemed consistent with the ^{13}C NMR data, and it should be expected according to the syn-directing effect of the hydroxyl group and the steric effects. The epoxidation of 11 with m-chloroperbenzoic acid afforded also a single product (16) in 77% yield. The ^{13}C NMR spectrum of 16 exhibited a shielding effect on the signal assigned to C-9 (when it was compared with the spectrum of 11). This was consistent with an α-configuration of the oxirane ring. In addition, when diol 11 was epoxidized with t-butylhydroperoxide in the presence of vanadyl acetyl acetonate[15], the same product 16 was also isolated (53%), and this is consistent with the stereochemistry assigned to the oxirane ring. Another compound obtained from this reaction was the ketodiol (12) (see above). This product was possibly an artifact formed during the separation process on a silicagel column[16] since its presence was not detected during the t. l. c. analysis of the crude reaction product. The cis arrangement of the vicinal diol system of 12 was supported by ^{13}C NMR data obtained in the presence of boric acid[13].

In order to gather further chemical evidence for the anomalous cis arrangement of the hydroxyl groups in compound 5 as well as to establish a procedure to functionalize selectively one of the double bonds of 1 we carried out the following sequence.



11 16 (77%) 20 (87%) 5 (66%)

Compound 16 was oxidized with chromium trioxide-pyridine complex to afford the corresponding 7-keto-derivative 20 in fairly good yield (87%). Treatment of 20 with trimethyl silyl chloride and aqueous hydrazine in dimethyl formamide[16] gave compound 5 with a reasonable yield (66%). The application of this procedure to the mixture of 1,4-diols (9) obtained by the epoxidation of 1 with m-CPBA in tetrahydrofuran : water (10 : 1) would allow us (see Experimental) to transform these major reaction products into a mixture of 13,14-diols (6) in a multigram scale. This last product (6) could be used, eventually, to prepare sesquiterpenes of the drimane type[20].



9 14 15 6

Table 2. ^{13}C NMR chemical shifts (ppm) for epoxide compounds (2, 3, 17, 18 and 19)

	2	3	17	18	19
C-1	37.8	38.8	38.4	39.4	38.4
C-2	18.1	18.0	17.9	17.4	17.9
C-3	37.3	37.0	36.8	37.4	36.8
C-4	46.7	46.5	46.3	46.5	46.3
C-5	45.4	44.2	39.9	44.0[c]	39.7
C-6	26.0	25.3[b]	23.0[b]	23.9[b]	23.0[b]
C-7	129.7	127.6	58.6	59.0	57.8
C-8	133.0	134.3	55.4	59.8	57.5
C-9	50.7	47.5	49.3	44.4[c]	46.3
C-10	34.6	34.6	34.0	34.7	35.6
C-11	16.6	22.8	15.8	20.5	17.7
C-12	26.0	25.6[b]	24.4[b]	24.7[b]	24.4[b]
C-13	64.2	66.7	63.0	65.0	65.3
C-14	60.9	62.8	62.2	62.2	62.3
C-15	34.0	35.4	33.1	35.1	33.5
C-16	17.7[a]	17.4[a]	17.5[a]	17.1[a]	17.7[a]
C-17	18.1[a]	18.1[a]	17.9[a]	18.0[a]	17.9[a]
C-18	178.9	178.8	178.2	178.7	178.3
C-19	16.8	17.0	17.5	16.8	17.5
C-20	14.1	14.3	15.4	15.4	16.0
C-21	51.8	51.9	51.8	51.9	52.0

a, b and c Reversed assignment is also possible.

EXPERIMENTAL

Methyl abietate (1) used in this work was obtained through methylation of commercial abietic acid (Fluka) with diazomethane in ethyl ether solution at -24° C and filtration through silica gel (hexane : ethyl acetate, 9 : 1) or neutral alumina (hexane : ethyl acetate, 99 : 1). Column chromatography was done either on silica gel 60, 70-230 mesh (Merck) or neutral alumina, (IV, 70-230 mesh (Merck), as referred; t.l.c. was carried out on plates of silica gel $60F_{254}$ (Merck). ^1H NMR spectra and ^{13}C NMR spectra were measured with a Varian 390 (90 MHz) and either a Bruker WP-80 (20.1 MHz) or WP-360 (90.5 MHz) spectrometers respectively in $CDCl_3$ solution with tetramethylsilane as internal reference. Assignments of ^{13}C NMR shifts were made with the aid of off-resonance and noise decoupled ^{13}C NMR spectra. M.p.s were determined in a Kofler hot-stage apparatus. Optical rotations were measured in chloroform solutions unless otherwise stated with a Perkin-Elmer 141 polarimeter.

Reaction of methyl abietate with m-chloroperbenzoic acid. (a) With one equiv. in dichlorometane. To a stirred solution of methyl abietate (1) (548 mg, 1.73 mmol) in dichloromethane (10 ml) at 0° C m-chloroperbenzoic acid (309 mg, 1.79 mmol), was added as a single portion. The mixture was stirred for 5.0 h and then washed with a solution of sodium metabisulphite, water, saturated sodium hydrogen carbonate solution and water again. Solvent was removed under pressure to give a syrup which was then chromatographed on neutral alumina (50 g). Elution with hexane afforded a mixture of at least three products (^{13}C NMR) with the same R_F and showing UV absorption (44 mg). Further elution with hexane : ethyl acetate (98 : 2) afforded methyl 13 β, 14 β-epoxyabiet-7-en-18-oate (2) (60 mg, 10%); m.p. 60-62° C, $[\alpha]_D$ +0.3° (c 5.74); δ_H 5.80 (1H, m, W ½ 9 Hz, 7-H), 3.65 (3H, s, OCH_3), 3.10 (1H, s, 14-H), 1.20 (3H, s, 4-Me), 1.00 and and 0.97 (6H, 2d, J 7 Hz, 15-Me_2), 0.80 (3H, s, 10-Me); (Found: C, 75.86; H, 9.36;

$C_{21}H_{32}O_3$ requires: C, 75.86; H, 9.70%) and methyl 13 α, 14 α-epoxyabiet-7-en-18-oate (3) (25 mg, 4%); m.p. 66-70° C; $[\alpha]_D$ -4.5° (c 1.33 in CH_2Cl_2); δ_H 5.90 (1H, m, W½ 6 Hz, 7-H), 3.60 (3H, s, OCH_3), 3.10 (1H, s, 14-H), 1.25 (3H, s, 4-Me), 0.95 and 0.93 (6H, 2d, J 7 Hz, 15-Me_2), 0.75 (3H, s, 10-Me); (Found: C, 75.47; H, 9.51; $C_{21}H_{32}O_3$ requires: C, 75.86; H, 9.70%) along with a mixture of 2 and 3 (30 mg, 5%).

(b) With one equiv. in dichloromethane in the presence of anhydrous sodium carbonate (1 equiv.). To a stirred solution of methyl abietate (1) (204 mg, 0.64 mmol) in dichloromethane (10 ml) at -8° C anhydrous sodium carbonate (75 mg, 0.71 mmol), and m-CPBA (122 mg, 0.71 mmol), were added as single portions. The resulting solution was stirred for 7.0 h and then worked up as above. Chromatography of the crude product in neutral alumina under the previous conditions afforded 2 and 3 as a mixture (57 mg, 27%) which was not rechromatographed.

(c) With one equiv. in dichloromethane in the presence of KF (two equiv.). To a suspension of freshly activated KF (86 mg, 1.48 mmol) (1 h, 110° C, 1 mm Hg) in 2.8 ml of dry dichloromethane, m-CPBA (128 mg, 0.74 mmol) was added. The mixture was stirred for 30 min at -24° C (dry ice, CCl_4) and then methyl abietate (1) (180 mg, 0.57 mmol) in CH_2Cl_2 (3 ml) was added. The reaction mixture was kept with stirring for 24 h at the same temperature, filtered off, dried under vacuum and the resulting syrup chromatographed as above to yield 2 and 3 (66 mg, 34%).

In all these cases, besides the monoepoxides, variable amounts of UV absorbing substances (dehydroabietic acid methyl ester and a mixture of dienes; ^1H and ^{13}C NMR), m-chlorobenzoyloxy-derivatives (^1H NMR) and diepoxides (t.l.c.), were detected.

(d) With one equiv. in tetrahydrofuran : water (10 : 1). To a stirred solution of methyl abietate (1) (1.450 g, 4.6 mmol) in THF : H_2O (10 : 1) (165 ml) at 0° C, m-CPBA (949 mg, 5.5 mmol) was added as a single portion. The reaction was kept with stirring for 36 h. No major change in the composition of the reaction mixture was observed after 20 h. Five main spots were detected (t.l.c.) [hexane : ethyl acetate (8 : 2) and then hexane : ethyl acetate (1 : 1)]. Work up was carried out as usual. Separation was achieved by chromatography in neutral alumina. Elution with hexane afforded a mixture of UV absorbing substances dienes and dehydroabietic acid methyl ester (284 mg, 19%) (t.l.c., ^1H NMR). Further elution with hexane : ethyl acetate (98 : 2) gave a mixture of the monoepoxides 2 and 3 (340 mg, 22%) (t.l.c., ^1H NMR). Elution with hexane : ethyl acetate (9 : 1) afforded compound 4 (50 mg, 5%) slightly impurified with m-chlorobenzoyloxy-derivatives (t.l.c., ^1H NMR). Elution with hexane : ethyl acetate (7 : 3) afforded compounds 7 and 5 as a mixture which after chromatographic separation gave 7 (433 mg, 27%) and 5 (97 mg, 6%). Finally, elution with hexane : ethyl acetate (2 : 8) gave compound 11 (244 mg, 15%) (see below).

Solvolysis of compound 2 in t-butanol. To a stirred solution of epoxide 2 (293 mg, 0.92 mmol) in t-butanol (30 ml) at 0° C, 0.6 ml of a 0.12 N perchloric acid solution was added. The resulting solution was stirred for 20 min and then sodium hydrogen carbonate (75 mg) was added. The reaction mixture was then diluted with water and extracted with ether (50 ml). The organic phase was washed with saturated sodium chloride solution, water, dried over anhydrous magnesium sulfate and evaporated under vacuum. Chromatography of the resulting crude product on alumina (50 g) beginning with ethyl acetate : hexane (2 : 98) afforded, in order of increasing polarity: Methyl 7 α-butoxy-13 ß-hydroxy-abiet-8(14)-en-18-oate (8) (123 mg, 37%), syrup, $[\alpha]_D$ -13.3 (c 2.10); δ_H 5.55 (1H, br s, W½ 3 Hz, 14-H), 3.90 (1H, m, W½ 6 Hz, 7-H), 3.65 (3H, s, OCH_3), 1.20 (3H, s, 4-Me), 1.10 (9H, s, $-OC(CH_3)_3$), 0.92 and 0.90 (6H, 2d, J 7 Hz, 15-Me_2), 0.75 (3H, s, 10-Me); methyl 13 ß, 14 α-dihydroxy-abiet-7-en-18-oate (4) (29 mg, 9%), oil, $[\alpha]_D$ -6.1° (c 4.09); δ_H 5.75 (1H, m, W½ 9 Hz, 7-H), 3.85 (1H, s, 14-H), 3.65 (3H, s, OCH_3), 1.25 (3H, s, 4-Me), 1.00 and 0.97 (6H, 2d, J 7 Hz, 15-Me_2), 0.85 (3H, s, 10-Me); and methyl 13 ß, 7 α-dihydroxy-abiet-8(14)-en-oate (7) (93 mg, 33%) (white needles from hexane : ethyl acetate), m.p. 109-111° C, $[\alpha]_D$ -18.1° (c 3.15); δ_H 5.70 (1H, m, W½ 3 Hz, 14-H), 4.20 (1H, m, W½ 9 Hz, 7-H), 3.70 (3H, s, OCH_3), 1.20 (3H, s, 4-Me), 0.97 and 0.90 (6H, 2d, J 7 Hz, 15-Me_2), 0.85 (3H, s, 10-Me). (Found: C, 72.02; H, 10.28; $C_{21}H_{34}O_4$ requires: C, 71.96; H, 9.78%).

Solvolysis of compound 3 in t-butanol. As described above: Epoxide 3 (218 mg) was stirred in t-butanol : $HClO_4$ 0.12 N solution (98 : 2 v/v) at 0° C for 90 min. Then sodium hydrogen carbonate (75 mg) was added. After the corresponding work up, chromatography on neutral alumina with hexane : ethyl acetate (98 : 2) afforded methyl 7 α-t-butoxy-13 α-hydroxy abiet-8 (14)-en-18-oate (10), (100 mg, 35%), syrup, $[\alpha]_D$ -48° (c 2.46); δ_H 5.55 (1H, br s, W½ 3 Hz, 14-H), 3.95 (1H, m, W½ 9 Hz, 7-H), 3.65 (3H, s, OCH_3), 1.15 (12 H, s, 4-Me and $-OC(CH_3)_3$), 0.95 and 0.92 (6H, 2d, J 7 Hz, 15-Me_2), 0.87 (3H, s, 10-Me). Further elution with hexane : ethyl acetate (9 : 1) gave compound 5: Methyl 13 α - 14 α-dihydroxy-abiet-7-en-18-oate, (37 mg, 15.4%), solid (white needles from hexane : ethyl acetate) m.p. 134-136° C, $[\alpha]_D$ +3.0 (c 2.31); δ_H 5.70 (1H, m, W½

9 Hz, 7-H), 4.00 (1H, s, 14-H), 3.62 (1H, s, OCH_3), 1.25 (3H, s, 4-Me), 0.92 (6H, d, 7 Hz, 15-Me_2), 0.80 (3H, s, 10-Me). (Found: C, 71.94; H, 10.25; $C_{21}H_{34}O_4$ requires: C, 71.96; H, 9.78 %.).

Hydrolysis of epoxide 3 in tetrahydrofuran: water with $HClO_4$ as catalyst. Diluted perchloric acid (0.12 N, 10 drops) was added to a solution containing epoxide 3 (300 mg) in tetrahydrofuran (20 ml) and water (2 ml) and kept with stirring at 0° C. After 10 h at 0° C sodium hydrogen carbonate was added and the resulting solution diluted with water and extracted with ethyl ether. The organic layer was washed with saturated sodium hydrogen carbonate solution, water, dried over $MgSO_4$ and chromatographed on neutral alumina to afford in order of elution: Compound 5 (55 mg, 16%) [hexane: ethyl acetate (9:1)] and compound 11 (148 mg, 49%): Methyl 7α, 13α-dihydroxyabiet-8 (14)-en-18-oate as a solid m.p. 115-118° C, $[\alpha]_D$ -66.0 (c 8.36); δ_H 5.65 (1H, br s, W ½ 3 Hz, 14-H), 4.15 (1H, m, W ½ 6 Hz, 7-H), 3.65 (3H, s, OCH_3), 1.20 (3H, s, 4-Me), 1.00 and 0.97 (6H, 2d, J 7 Hz, 15-Me_2), 0.85 (3H, s, 10-Me), characterized as its 7α-acetoxy-derivative (Ac_2O. Py, 48 h, r.t.) solid (white needles from hexane) m.p. 120-121° C, $[\alpha]_D$ -34.4 (c 3.63); δ_H 5.80 (1H, s, 14-H), 5.20 (1H, br s, W ½ 6 Hz, 7-H), 3.60 (3H, s, OCH_3), 2.00 (3H, s, $OCOCH_3$), 1.15 (3H, s, 4-Me), 0.90 and 0.87 (6H, 2d, J 7 Hz, 15-Me_2), 0.80 (3H, s, 10-Me). ^{13}C NMR (ppm)[18]: C-1 38.0 (t), C-2 18.1 (t), C-3 36.9 (t), C-4 47.0 (s), C-5 42.8 (d), C-6 30.0 (t), C-7 75.3 (d), C-8 136.1 (s), C-9 46.6 (d), C-10 38.3 (s), C-11 18.1 (t), C-12 31.5 (t), C-13 71.7 (s), C-14 135.4 (d), C-15 36.0 (d), C-16 16.7 (q), C-17 16.7 (q), C-18 178.5 (s), C-19 16.7 (q), C-20 14.7 (q), C-21 51.8 (q), $OCOCH_3$ 170.2 (s), $OCOCH_3$ 21.45 (q). (Found: C, 70.79; H, 9.73; $C_{21}H_{36}O_5$ requires: C, 70.37; H, 9.24%).

Reaction of compound 8 with m-CPBA. Compound 8 (230 mg, 0.56 mmol) in $CHCl_3$ (10 ml) at 0° C was treated with m-CPBA (130 mg, 0.75 mmol, 1.3 equiv.) for 24 h at 0° C. After the usual work up and filtration through neutral alumina methyl 7α-t-butoxy-13β-hydroxy-8β, 14β-epoxyabietan-18-oate (13) (210 mg, 88%) was isolated. Amorphous solid, $[\alpha]_D$ -23.1 (c 1.21); δ_H 3.65 (3H, s, OCH_3), 3.10 (1H, m, W ½ 6 Hz, 7-H), 2.70 (1H, s, 14-H), 1.20 (3H, s, 4-Me), 1.17 (9H, s, $OC(CH_3)_3$), 1.00 and 0.98 (6H, 2d, J 7 Hz, 15-Me_2), 0.93 (3H, s, 10-Me). (Found: C, 70.75; H, 10.02. $C_{25}H_{42}O_5$ requires: C, 71.05; H, 10.02%).

Reaction of compound 11 with m-CPBA. To a stirred solution of dihydroxycompound 11 (235 mg, 0.67 mmol) in $CHCl_3$ (20 ml) at 0° C m-CPBA (151 mg, 0.87 mmol) was added as a single portion. The solution was kept at 0° C for 12 h and then more m-CPBA (55 mg, 0.5 equiv.) was added. After six more hours the reaction was worked up as usual and the crude product filtered through a column of silica gel using hexane: ethyl acetate (8:2) as eluent. Methyl 7α, 13α-dihydroxy-8α, 14α-epoxyabietan-18-oate (16) (189 mg, 77%), syrup, $[\alpha]_D$ -40.9 (c 2.69); δ_H 3.65 (3H, s, OCH_3), 3.42 (1H, m, W ½ 6 Hz, 7-H), 3.10 (1H, s, 14-H), 1.20 (3H, s, 4-Me), 1.00 and 0.93 (6H, 2d, 15-Me_2), 1.00 (3H, s, 10-Me) was isolated.

Reaction of compound 11 with ter-butylhydroperoxide/V^{5+}. To a stirred solution of compound 11 (297 mg, 0.85 mmol) and vanady acetyl acetonate (6.8 mg, 0.026 mmol)[19] in dry toluene (10 ml) at 0° C was added dropwise anhydrous terbutylhydroperoxide in toluene (0.6 ml, 2 mmol). The reaction was monitored by t.l.c. and judged complete after 6 h at 0° C (only one spot was observed). Freshly prepared 10% solution of sodium sulfite (Na_2SO_3) was added dropwise with stirring. When addition was complete the ice bath was removed and stirring continued for 3 h at room temperature. The aqueous and organic phases were separated and the organic layer washed twice with water, brine and water again, dried over anhydrous magnesium sulfate and concentrated to afford a syrup which was dissolved in $CHCl_3$ and chromatographed in silica gel to yield two compounds: Methyl 13α, 14α-dihydroxy-7-oxoabietan-18-oate (12) (50 mg, 17%), solid m.p. 186-190° C, $[\alpha]_D$ 19.5 (c 1.28); δ_H 4.3 (1H, br s, W ½ 6 Hz, 14-H), 3.65 (3H, s, OCH_3), 1.20 (3H, s, 4-Me), 1.05 (3H, s, 10-Me), 0.95 and 0.90 (6H, 2d, J 7 Hz, 15-Me_2), and 16 (165 mg, 53%).

Reaction of compound 2 with m-CPBA. To a stirred suspension of epoxide 2 (213 mg, 0.64 mmol) and anhydrous Na_2CO_3 (95 mg, 0.89 mmol) in freshly distilled and dried CH_2Cl_2 (10 ml) at 0° C m-CPBA (133 mg, 0.77 mmol) was added as a single portion. After 20 h the reaction was not complete (t.l.c.) and more Na_2CO_3 (27 mg, 0.4 equiv.) and m-CPBA (44 mg, 0.4 equiv.) were added. Usual work up and chromatography of the crude [neutral alumina, hexane: ethyl acetate (98:2)] afforded diepoxide 17: Methyl 7α, 8α, 13β, 14β-diepoxy-abietan-18-oate (164 mg, 73.5%), m.p. 55-58° C, $[\alpha]_D$ -10.2 (c 1.86); δ_H 3.65 (3H, s, OCH_3), 3.15 (1H, br s, W ½ 4.5 Hz, 7-H), 2.25 (1H, s, 14-H), 1.20 (3H, s, 4-Me), 1.00 and 0.95 (6H, 2d, J 7 Hz, 15-Me_2), 0.85 (3H, s, 10-Me). (Found: C, 72.17; H, 9.40. $C_{21}H_{32}O_4$ requires: C, 72.37; H, 9.25%).[21]

Reaction of compound 3 with m-CPBA. Epoxide 3 (209.8 mg, 0.63 mmol) was treated under the conditions depicted above with m-CPBA (130.7 mg, 0.75 mmol) and Na_2CO_3 (100 mg, 0.94 mmol) for 17 h. As compound 3 was still present in the reaction mixture (t.l.c.), two sucessive

portions of 0.5 equiv. of m-CPBA and Na_2CO_3, along with 5 ml of CH_2Cl_2, were added and the reaction further kept at 0° C for 9 h. After the usual work up and chromatography in neutral alumina of the crude mixture, two compounds were isolated. Eluting with hexane:ethyl acetate (98 : 2) gave compound 18: Methyl 7β, 8β, 13α, 14α-diepoxy-abietan-18-oate (54 mg, 24 %), syrup, (white needles from hexane at -20° C), m.p. 86-88° C, $[\alpha]_D$ -24.9 (c 2.85); δ_H 3.65 (3H, s, OCH_3), 3.25 (1H, d, J 6 Hz, 7-H), 2.30 (1H, s, 14-H), 1.15 (3H, s, 4-Me), 1.00 and 0.95 (6H, d, J 7 Hz, 15-Me_2), 0.85 (3H, s, 10-Me). (Found: C, 72.29; H, 9.76. $C_{21}H_{32}O_4$ requires: C, 72.38; H, 9.26 %). Further elution with hexane : ethyl acetate (96.5 : 3.5) yielded methyl 7α, 8α, 13α, 14α-diepoxy-abietan-18-oate (19) (115 mg, 52 %);[21] amorphous solid, (white needles from hexane : ethyl acetate), m.p. 150-153° C, $[\alpha]_D^+$ 52.9 (c 2.27); δ_H 3.50 (3H, s, OCH_3), 3.00 (1H, br s, W ½ 4.5 Hz, 7-H), 2.30 (1H, s, 14-H), 1.15 (3H, s, 4-Me), 0.90 and 0.85 (6H, 2d, J 7 Hz, 15-Me_2), 0.80 (3H, s, 10-Me). (Found: C, 72.50; H, 9.77. $C_{21}H_{32}O_4$ requires: C, 72.38; H, 9.26 %).

Oxidation of compound 16 with CrO_3.2Py. Pyridine (10 ml, 124 mmol, 18 equiv.) was added to a stirred suspension of CrO_3 (dried over P_2O_5, 130° C, 1 mm Hg, 5 h) (6.2 g, 62.0 mmol, 9 equiv.) in CH_2Cl_2 (distilled over P_2O_5 and stored under Ar) (100 ml) under Ar. The resulting solution was stirred for 30 min, and the epoxide compound 16 (2.4 g, 6.89 mmol) in CH_2Cl_2 (30 ml) was added in a single portion. After stirring for 2 h at r.t. more CH_2Cl_2 (100 ml) was added and the resulting mixture decanted and washed three times with 10 % aqueous NaOH solution (250 ml), three times with 5 % aqueous HCl solution (200 ml) and once with brine (250 ml). The extract was dried (Na_2CO_3) and filtered through a column of Florisil (eluting with CH_2Cl_2). After evaporation of the solvents compound 20: Methyl 13α-hydroxy-8α, 14α-epoxy-7-oxo-abietan-18-oate (2.060 g, 87 %) was obtained (crystals from hexane : ethyl acetate), m.p. 143-145° C; $[\alpha]_D$ -139.3 (c 5.21); δ_H 3.60 (3H, s, OCH_3), 3.45 (1H, s, 14-H), 1.20 (3H, s, 4-Me), 1.00 and 0.93 (6H, d, J 7 Hz, 15-Me), 0.85 (3H, s, 10-Me). (Found: C, 69.43; H, 9.03; $C_{21}H_{32}O_5$ requires: C, 69.20; H, 8.85 %).

Reaction of 20 with $NH_2NH_2.H_2O$. Trimethylsilyl chloride (1 ml, 6.84 mmol, 3 equiv.) was added to a solution of keto-epoxy compound 20 (828 mg, 2.28 mmol) and hydrazine hydrate (0.55 ml, 11.4 mmol, 5 equiv.) in anhydrous DMF (18 ml) and the resulting solution under Ar was stirred at r.t. for 2 h. The reaction mixture was then diluted with water (30 ml) and extracted with ether (3 x 50 ml), and the combined organic extracts washed with brine (150 ml) and dried ($MgSO_4$). Evaporation of the solvent and flash chromatography of the crude [hexane : ethyl acetate, (25 : 75)] afforded 528 mg (66 %) of a compound which showed to be identical (^1H NMR, ^{13}C NMR, m.p.) to the previously obtained diol 5.

Epoxidation of compounds 9 (7 + 11) with m-CPBA. A mixture of compounds 9 was treated as described above for 24 h in $CHCl_3$ at 0° C and after the usual work up yielded compounds 14 in a virtually quantitative yield.

Oxidation of compounds 14 with CrO_3.2Py in dichloromethane. Compounds 14 (6.7 g) were oxidized as indicated above, yielding compounds 15 as a white solid (5.4 g, 81 %) which without further purification was used in the Wharton rearrangement step.

Obtention of diols 6 (4 + 5). The Wharton procedure (see above) was applied to the mixture of epoxides 15 (235 mg, 0.6 mmol), yielding a mixture of diols 6 (115 mg, 51 %).

Oxidation and hydrolysis of compound 4. A solution of pyridinium chlorochromate (275 mg, 3 equiv.), anhydrous sodium acetate (90 mg) and molecular sieves (4 Å) in dry CH_2Cl_2 (10 ml) stirred for 30 min was poured over a solution of the diol 4 (103 mg, 0.437 mmol) in dry CH_2Cl_2 (5 ml). After 45 min ethyl ether was added and the resulting solution filtered through a silicagel pad (60 G Merck), the residue was washed with ethyl ether and the solvents evaporated to afford a syrup which was subjected to flash chromatography to give methyl 13 8-hydroxy-14-oxo-abiet-7-en-18-oate (30 mg). δ_H 7.00 (1H, m, W ½ 8 Hz, 7-H), 3.66 (3H, s, OCH_3), 1.25 (3H, s, 4-Me), 0.92 (6H, d, J 7 Hz, 15-Me_2), 0.77 (3H, s, 10-Me) which was treated with 3N KOH (0.150 ml) in DMSO (0.850 ml) for 2 h at r.t. to yield, after usual work up and flash chromatography of the crude, 13 8-hydroxy-14-oxo-abiet-7-en-18-oic acid (9 mg), m.p. 186-189° C, from ether-hexane (lit[24] m.p. 189-190° C).

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REFERENCES AND NOTES

1. J. Escudero, C. Márquez, R.M. Rabanal and S. Valverde, Tetrahedron, 1983, 39, 3167.
2. a) E. Glotter and M. Zviely, J. Chem. Soc. Perkin Trans. I, 1984, 2345; b) R.C.Cambie, Ch. M. Read, P.S. Rutledge, G.J. Walker, P.D. Woodgate and J.R. Hanson, J. Chem. Soc. Perkin Trans. I, 1980, 2581; c) C. Djerassi, A.J. Lemin, G. Rosenkranz and E. Sondheimer, J. Chem. Soc., 1954, 2346.
3. B.A. Arbuzov and A.G. Khismatullina, Izv. Akad. Nauk. SSSR, Khim. Nauk., 1961, 1280, C.A. 56, 1485c.
4. M. Korach, D.R. Nielsen and W.H. Rideout, J. Am. Chem. Soc., 1960, 82, 4328.
5. A. Enoki and K. Kitao, Mokuzai Gakkaishi, 1975, 21, 101, C.A. 83, 81660d.
6. Y. Miki, K. Hideo, C.A., 1980, 92, 129123w.
7. a) Yu. A. Cilco, V.A. Raldugin, V.I. Mamatyuk, E.N. Shmidt and V.A. Pentegova, Izv. Sib. Otd Akad. Nauk. SSSR, Khim. Nauk., 1983, 124, C.A. 1983, 99, 83399f; b) Yu. A. Cilco, V.A. Raldugin, E.N. Schmidt, V.I. Mamatyuk and V.A. Pentegova, C.A., 1984, 101, 152129r.
8. a) K. Tori, T. Komeno, M. Sangare, B. Septe, B. Delpech, A. Ahond and G. Lukacs, Tetrahedron Lett., 1974, 1157; b) B. Papillaud, F. Tiffon, M. Taran, B. Arreguy-San Miguel and B. Delmond, Tetrahedron, 1985, 1845; c) B. Delmond, B. Papillaud, J. Valade, M. Petraud and B. Barbe, Org. Magn. Reson., 1979, 12, 209.
9. F. Camps, J. Coll, A. Messeguer and F. Pujol, J. Org. Chem., 1982, 47, 5402.
10. R.Y.S. Tan, R.A. Russell and R.N. Warrener, Aust. J. Chem., 1981, 34, 421, and references therein.
11. B. Delmond, M. Taran, J. Valade, M. Petraud and B. Barbe, Org. Magn. Reson., 1981, 17, 207.
12. W. Cocker, K.J. Crowley and K. Srinivasan, J. Chem. Soc. Perkin Trans. I, 1973, 2485.
13. F. Fernández-Gadea, M.L. Jimeno and B. Rodríguez, Org. Magn. Reson., 1984, 22, 515, and references therein.
14. S.A. Cerecife and E.K. Fields, J. Org. Chem., 1976, 41, 355.
15. Sh. Tanaka, H. Yamamoto, H. Nozaki, K.B. Sharpless, R.C. Michaelson and J.C. Cutting, J. Am. Chem. Soc., 1974, 96, 5254.
16. J.W. Apsimon and S.F. Hall, Can. J. Chem., 1978, 56, 2156.
17. D.D. Maas, M. Blagg and D.F. Wiemer, J. Org. Chem., 1984, 49, 853.
18. E. Wenkert, M.J. Gasic, E. W. Hagaman and L.D. Kwart, Org. Magn. Reson., 1975, 7, 51.
19. J.G. Hill, B.E. Rossiter and K.B. Sharpless, J. Org. Chem., 1983, 48, 3067.
20. H. Okawara, H. Nakai and M. Ohno, Tetrahedron Lett., 1982, 23, 1087.
21. Compounds: 7, 11, 17 and 19 have been already described [7a] although, as previously indicated for epoxides 2 and 3, the stereochemistry assigned to C-13 is the opposite in each compound to that assigned in this communication. We should also point out that optical rotations of some of these compounds is just of opposite sign to that published [7a].
22. Though compound 5 has been prepared (see ref. 20) by OsO_4 treatment of abietic acid no data has been reported.
23. Literature data for epoxides 2 and 3 [7a]: M.p. 67-69° C and 58-59° C, respectively.
24. B.E. Cross and P.L. Myers, J. Chem. Soc. (C), 1969, 711.